REMARKS

I. Status of Claims

Claims 1-46 were filed with the application. Claims 4, 15 and 25-46 stand withdrawn. Thus, claims 1-3, 5-14 and 16-24 remain pending, have been examined, and stand rejected, variously, under 35 U.S.C. §112, second paragraph, 35 U.S.C. §112, first paragraph, 35 U.S.C. §102, and 35 U.S.C. §103. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Sequence Compliance

The examiner has identified sequences at page 48 (lines 12-13) and page 51 (lines 28-29) that do not have corresponding SEQ ID NOs associated with them. An amendment and substitute sequence listing are provided herewith correcting the deficiency.

III. Oath and Declaration

The oath/declaration is said to be defective in lacking a ***dated*** signature for Gregory Evans. Applicants are in the process of obtaining a replacement oath/declaration, which will be submitted shortly.

IV. Objections

Claim 5 is objected to because of a misspelling. Claim 14 is objected to due to a grammatical errors. Both have been corrected by amendments. Reconsideration and withdrawal of the objections is therefore respectfully requested.

V. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 2, 9, 11, 12 and 19-24 stand rejected under the second paragraph of §112, as indefinite. The individual rejections are addressed below:

Claim 2: The examiner argues that the citation of a series of cells does not indicate whether all of these cells are part of the same conduit, or used individually. An amendment replacing "and" with "or" has been provided. However, given that claims 1 and 2 use the term "comprising," the use of "or" does not preclude the presence of other cell types.

Claims 9, 11 and 12: The examiner argues that the use of the term "gene" is inconsistent with the subsequent recitation of a gene product, *i.e.*, a polypeptide. A clarifying amendment is provided.

Claims 19-24: The term "induction" in claims 19-24[1] is said to lack antecedent basis. Amendments have been provided to address the rejection.

In light of the preceding, applicants believe that each ground of rejection has been addressed. Therefore, reconsideration and withdrawal of the rejections is respectfully requested.

VI. Rejection Under 35 U.S.C. §112, First Paragraph (Written Description)

Claims 8-14 are rejected under the first paragraph of §112 as allegedly lacking a legally sufficient written description. According to the examiner, the specification is deficient in not describing "cell kill genes" given the unpredictability in the art and the lack of a correlation between structure and function. Applicants traverse.

[1] Claim 19 does not contain the limitation "induction." Thus, rejection of this claim is believed to be an error.

The examiner has not stated any rational basis for challenging the generic disclosure of "cell kill genes." First and foremost, there is no "structure-function" relationship between various cell kill genes given that they are quite distinct in how they accomplish their role in killing of cells. Thus, it is non-sensical in this context to suggest that such is required. Moreover, it also makes no sense to require a detailed discussion of genomic clones, including introns and regulatory sequences, since there is nothing in the specification, and nothing provided in the Office Action, to indicate that these elements are in any way required for the present invention. Finally, the examiner's comments on "herbicide tolerance genes" are not understood.

The only relevant issue raised by the examiner is whether "cell kill genes" as a genus were known at the time of filing. Applicants submit that the specification, which identifies (a) regulated expression of toxins and (b) enzyme/prodrug combinations, shows that cell kill genes clearly were known. The specific example of HSV-tk is provided for the latter type of cell kill gene. See Specification, paragraph bridging pages 4-5. As such, there is little questions that a genus of "cell kill genes" was supported at the time of filing.

In light of the foregoing, applicants respectfully request reconsideration and withdrawal of the rejection.

VII. Rejection Under 35 U.S.C. §112, First Paragraph (Enablement)

Claims 1-33 are rejected under the first paragraph of §112 as allegedly lacking an enabling disclosure.[2] The examiner has provided an analysis of five different Wands factors; as such, the analysis is incomplete. Moreover, the examiner has cited no evidence to support

[2] Claims 25-33 have been withdrawn and are canceled herein. It is believed that their inclusion in this rejection was in error.

factual assertions that (a) the state of the art is devoid of clinical success, (b) that there is a "lack of methods steps for use of the [present] invention," (c) that the art of nerve repair is unpredictable, (d) that there is a lack of correlation between the experimental model used and the claimed invention. Thus, in essence, the examiner simply questions whether or not the claimed invention will work without any supporting evidence.

It is black letter law that the Patent Office must take appellants' specification as in compliance with enablement requirements unless there is reason to doubt "the objective truth" of the specification. Otherwise, there would be no need for appellants to go to the trouble and expense of supporting a "presumptively accurate disclosure." *In re Marzocchi*, 169 UPSQ 370 (CCPA 1971). The examiner further is requested to provide an affidavit under 37 C.F.R. §1.104(d)(2) as the rejection appears to be based solely on "facts within the personal knowledge of an employee of the Office." If no supporting evidence or affidavit is provided, it is requested that the rejection be withdrawn.

Furthermore, as described in the attached declaration under 37 C.F.R. §1.132 from Gregory R.D. Evans, the inventors have successfully identified suitable conduit material and created helper cells transformed with an inducible promoter that directs expression of a growth factor.[3] Thus, the critical steps in preparing materials for use in the claimed method have been accomplished, and there is no reason to doubt that such materials cannot be placed into a suitable animal. This is further evidence of enablement for the present invention.

In light of the foregoing, applicants respectfully submit that a *prima facie* case of non-enablement has not been established, but were such a case present, the evidence provided rebut even a valid *prima facie* rejection. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

VIII. Rejection Under 35 U.S.C. §102

Claims 1-7 are said to be anticipated by Hadlock *et al.* The reference is said to teach a neural regeneration conduit that is porous and can be comprised of PLGAS or PLLA. The conduit is said to include a layer of cells such as Schwann cells that can be engineered for the overexpression of neurotropic factors or NGF through recombinant expression. The conduits are said to be implanted into a subject adjacent to nerve tissues.

Claim 1 has now been amended to incorporate the elements of previous claim 4, namely, inducible expression of growth factors. The examiner has not pointed to any such disclosure in Hadlock, nor have applicants been able to identify any. As such, applicants believe the rejection of previous claim 4, and now claim 1, over Hadlock is improper. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

IX. Rejection Under 35 U.S.C. §103

Claims 1-7 and 15-18 are said to be rendered obvious by the combination of Hadlock in view of U.S. Patent 5,888,774 ("the '774 patent"). Hadlock is cited as above, but fails to disclose use of a recombinant vector for generation of cells to express a growth factor. The '774 patent is cited for the transformation of stem cells and fibroblasts using vectors with promoters and polyadenylation signals.

As an initial point, applicants challenge the rejection on the grounds that Hadlock, dealing with neural regeneration conduits, has little or no connection with the '774 patent, which is drawn to expression of erythropoietin, a compound that is of no relevance to nerve cells. Thus, there is no logical basis for the examiner's combination of the '774 patent with Hadlock.

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[3] Paragraph 7 of the declaration contains information that is not presented in the instant application.

The examiner states that column 13, line 64 reports the transformation of "stem cells and fibroblasts." This is utterly false. There is absolutely no mention of fibroblasts, and the reference teaches ***hematopoietic*** stem cells – clearly a far cry from nerve progenitors. In a valid §103 rejection, the reference must posit their own combination. *In re Vaeck*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Here, there is no such teaching.

Furthermore, as discussed above, claim 1 has now been amended to recite the elements of previous claim 4, namely, inducible expression of growth factors. Hadlock is silent on this feature. The '744 patent appears to mention, in passing, "inducible" promoters at column 9, line 27. However, as will be explained, there is insufficient motivation in Hadlock or the '744 patent to select truly "inducible" promoters as now claimed.

As explained in the present application, inducibility of a promoter is an important aspect of the invention in that it permits ***regulated*** expression of the growth factors that are needed to stimulate nerve growth, followed by removal of the stimulatory factor by withdrawal of the inducer. Much to the contrary, the '744 patent teaches on that "high level" expression is desired. See, *e.g.*, Column 3, line 38; Column 4, line 48-49; Column 9, line 12; Column 11, lines 1-2 and 52. In addition, it is also suggested that, in the particular situation of transgenic animals, tissue specific expression is desired, and that one way of achieving tissue specific expression is through the use of an inducible promoter. See Column 12, lines 29-67 and Column 12, lines 1-32. Thus, the thrust of the '744 patent is to achieve high expression, possibly in particular tissues, but without concern for any regulation. Thus, the notion of turning transgene expression on and off in a regulated fashion is not contemplated.

In light of these observations, applicants submit that there is no teaching or suggestion in the '774 patent to prepare a device comprising engineered nerve cells expressing, in an inducible

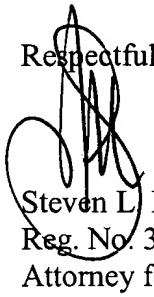
fashion, nerve cell growth factors. To the contrary, the overwhelming balance of the '774 patent is that high level expression is the ***only*** goal. As such, there were be no logical reason to read the '774 patent as teaching the benefits of inducible expression, and as admitted on the record, Hadlock had not even considered such an option, negating a possible suggestion from that reference.

In sum, the examiner has failed to establish that one of skill in the art, reading the citeed references, (a) would have any reason to combine the two cited references or (b) find any motivation to select the engineered nerve cells and conduits of Hadlock and combine them with an inducible promoter as mentioned (in passing) in the '774 patent. As such, there is no basis for alleging *prima facie* obviousness of the claims as presented for reconsideration.

X. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this response, a telephone call to the undersigned attorney at (512) 536-3184 is invited.

Respectfully submitted,



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Date: August 9, 2004